

(b) Z₄ is -C(O)- and R_{6a} is

(1) aryl optionally substituted with one or more Z₁, Z₂ or Z₃;

(2) alkyl optionally substituted with one or more Z₁, Z₂ or Z₃;

(3) cycloalkyl optionally substituted with one or more Z₁, Z₂ or Z₃; or

(4) heterocyclo optionally substituted with one or more Z₁, Z₂ or Z₃; or

(c) Z₄ is -C(O)-O- and R_{6a} is alkyl, cycloalkyl, aryl or aralkyl, any of which may be optionally substituted with one or more Z₁, Z₂ or Z₃.

17. A pharmaceutical composition comprising at least one compound of claim 7 and a pharmaceutically acceptable vehicle or carrier therefor.

REMARKS

Election/Restriction

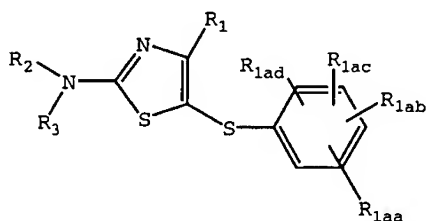
Applicants have cancelled claims 20-22, which are drawn to the non-elected invention of group II set forth in the Restriction requirement dated March 11, 2002.

Applicants appreciate the fact that the Examiner has found allowable subject matter after considering the elected species in view of the prior art. However, with respect to the "Generic Concept" set forth in the Examiner's action, Applicants respectfully submit that the Examiner's recasting of Applicants claimed invention is improper. Specifically, Applicants submit that the recasting of the claimed invention in terms of the "Generic Concept" set forth by the Examiner constitutes an improper refusal to examine that which the applicants regard as their invention. As explained in the MPEP:

Since the decisions in *In re Weber*, 580 F.2d 455, 198 USPQ 328 (CCPA 1978) and *In re Haas*, 580 F.2d 461, 198 USPQ 334 (CCPA 1978), it is improper for the Office to refuse to examine that which applicants regard as their invention, **unless the subject matter in a claim lacks unity of invention.** *In re Harnish*, 631 F.2d 716, 206 USPQ 300 (CCPA 1980); and *Ex parte Hozumi*, 3 USPQ2d 1059 (Bd. Pat. App. & Int. 1984). Broadly, unity of invention exists where compounds included within a Markush group (1) share a common utility, and (2) share a substantial structural feature disclosed as being essential to that utility.

MPEP §803.02 (emphasis added). Applicants submit that the pending claims do not lack “unity of invention”, and that the “Generic Concept” set forth by the Examiner, unduly narrows the scope of claims to which they are entitled.

Applicants have amended claim 7 to more definitively set forth a unified invention. Specifically, by limiting the definition of “Z” to –S–, applicants claim compounds of the following unified structure:



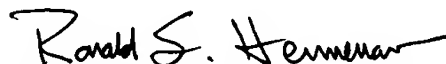
These compounds share both a common utility and a substantial structural core feature, and thus are “unified” for purposes of examination.

Applicants can find no provision in the Patent Statute, regulations or MPEP authorizing an Examiner to recast an applicant’s Markush claim in terms of a narrower “generic concept” as presently done by the Examiner on a first Office Action--after finding no invalidating prior art relating to the elected species. Indeed, in providing the Examiner with an elected species Applicants were of the understanding that the Examiner would be following the long-accepted procedure set forth mandated by MPEP §803.02, wherein the Markush claims are first fully examined with respect to the elected species, and then further (if no invalidating references are found) to the extent necessary to determine patentability.

Because the Examiner has located no invalidating references after examining the claims in view of the elected species, MPEP §803.02 requires further examination on the part of the Examiner to determine the patentability of Applicants’ markush claims.

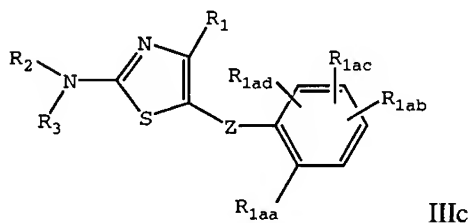
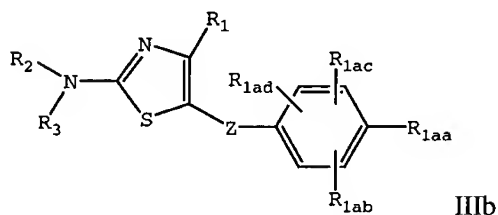
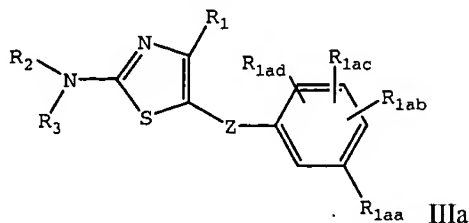
Respectfully submitted,

Bristol-Myers Squibb Company
Patent Department
P.O. Box 4000
Princeton, NJ 08543-4000
(609) 252-5781
Date: 8/9/02


Ronald S. Hermenau
Attorney for Applicants
Reg. No. 34,620

MARKED-UP VERSION OF AMENDED CLAIMS

7. A compound of formula IIIa, IIIb or IIIc



including diastereomers, enantiomers and salts thereof

where

Z is -S-

(1) ~~-O-~~

(2) ~~S-~~

(3) ~~CR₄R₆-O-CR_{4a}R_{6a}-~~

(4) ~~CR₄R₆-NR_{4b}-CR_{4a}R_{6a}-~~

(5) ~~CR₄R₆-S-CR_{4a}R_{6a}-~~

(6) ~~CR₄R₆-O-~~

(7) ~~CR₄R₆-NR_{4b}-~~

(8) ~~CR₄R₆-S-~~

(9) ~~S-CR₄R₆-~~

(10) ~~S(O)_q-~~

(11) ~~CR₄R₆-S(O)_q-~~ or

(12) ~~S(O)_q-CR₄R₆-~~

R₁, R_{1ab}, R_{1ac} and R_{1ad} are independently

- (13) hydrogen or R_6 ,
- (14) $-OH$ or $-OR_6$,
- (15) $-SH$ or $-SR_6$,
- (16) $-C(O)_qH$, $-C(O)_qR_6$, or $-O-C(O)_qR_6$, where q is 1 or 2,
- (17) $-SO_3H$ or $-S(O)_qR_6$,
- (18) halo,
- (19) cyano,
- (20) nitro,
- (21) $-Z_4-NR_7R_8$,
- (22) $-Z_4-N(R_9)-Z_5-NR_{10}R_{11}$,
- (23) $-Z_4-N(R_{12})-Z_5-R_6$, or
- (24) $-P(O)(OR_6)_2$;

R_{1aa} is $-C(O)_qH$, $-C(O)_qR_6$, $-Z_4-NR_7R_8$, $-Z_4-N(R_9)-Z_5-NR_{10}R_{11}$ or $-Z_4-N(R_9)-Z_5-R_6$;

R_2 and R_3 are each independently H, $-Z_4-R_{6a}$, or $-Z_4-NR_{7a}R_{8a}$;

R_4 , R_{4a} , R_5 and R_{5a} are each independently hydrogen, alkyl, aryl, aralkyl, cycloalkyl, or heteroarylalkyl;

R_6 , R_{6a} , R_{6b} and R_{6c} are independently alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl, cycloalkenylalkyl, aryl, aralkyl, heterocyclo, or heterocycloalkyl, each of which is unsubstituted or substituted with Z_1 , Z_2 and one or more groups Z_3 ,

R_7 , R_{7a} , R_8 , R_{8a} , R_9 , R_{10} , R_{11} and R_{12}

- (4) are each independently hydrogen, or $-Z_4R_{6b}$; or
- (5) R_7 and R_8 , or R_{7a} and R_{8a} may together be alkylene, alkenylene, or heteroalkylene, completing a 3- to 8-membered saturated or unsaturated ring with the nitrogen atom to which they are attached, which ring is unsubstituted or substituted with Z_1 , Z_2 and one or more groups Z_3 , or
- (6) any two of R_9 , R_{10} and R_{11} may together be alkylene, alkenylene or heteroalkylene completing a 3- to 8-membered saturated or unsaturated ring together with the nitrogen atoms to which they are attached, which ring is unsubstituted or substituted with one or more Z_1 , Z_2 and Z_3 ;

Z_1 , Z_2 and Z_3 are each independently

- (16) hydrogen or Z_6 ,
- (17) $-OH$ or $-OZ_6$,
- (18) $-SH$ or $-SZ_6$,
- (19) $-C(O)_qH$, $-C(O)_qZ_6$, or $-O-C(O)_qZ_6$,
- (20) $-SO_3H$, $-S(O)_qZ_6$, or $S(O)_qN(Z_9)Z_6$,
- (21) halo,
- (22) cyano,

- (23) nitro,
- (24) $-Z_4-NZ_7Z_8$,
- (25) $-Z_4-N(Z_9)-Z_5-NZ_7Z_8$,
- (26) $-Z_4-N(Z_{10})-Z_5-Z_6$,
- (27) $-Z_4-N(Z_{10})-Z_5-H$,
- (28) oxo,
- (29) any two of Z_1 , Z_2 , and Z_3 on a given substituent may together be alkylene or alkenylene completing a 3- to 8-membered saturated or unsaturated ring together with the atoms to which they are attached; or
- (30) any two of Z_1 , Z_2 , and Z_3 on a given substituent may together be $-O-(CH_2)_q-O-$;

Z_4 and Z_5 are each independently

- (10) a single bond,
- (11) $-Z_{11}-S(O)_q-Z_{12}-$,
- (12) $-Z_{11}-C(O)-Z_{12}-$,
- (13) $-Z_{11}-C(S)-Z_{12}-$,
- (14) $-Z_{11}-O-Z_{12}-$,
- (15) $-Z_{11}-S-Z_{12}-$,
- (16) $-Z_{11}-O-C(O)-Z_{12}-$,
- (17) $-Z_{11}-C(O)-O-Z_{12}-$; or
- (18) alkyl

Z_6 and Z_{6a} are independently

- (j) alkyl, hydroxyalkyl, alkoxyalkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl, cycloalkenylalkyl, aryl, aralkyl, alkylaryl, cycloalkylaryl, heterocyclo, or heterocycloalkyl;
- (iv) a group (i) which is itself substituted by one or more of the same or different groups (i); or
- (v) a group (i) or (ii) which is independently substituted by one or more of the groups (2) to (15) of the definition of Z_1 ;

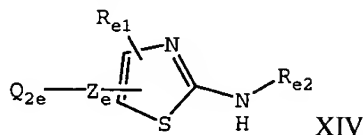
Z_7 , Z_8 , Z_9 and Z_{10}

- (4) are each independently hydrogen or $-Z_4-Z_{6a}$;
- (5) Z_7 and Z_8 may together be alkylene, alkenylene, or heteroalkylene completing a 3- to 8-membered saturated or unsaturated ring together with the atoms to which they are attached, which ring is unsubstituted or substituted with one or more Z_1 , Z_2 and Z_3 , or
- (6) Z_7 or Z_8 , together with Z_9 , may be alkylene, alkenylene, or heteroalkylene completing a 3- to 8-membered saturated or unsaturated ring together with the nitrogen atoms to which they are attached, which ring is unsubstituted or substituted with one or more Z_1 , Z_2 and Z_3 ;

Z_{11} and Z_{12} are each independently

- (5) a single bond,
- (6) alkylene,
- (7) alkenylene, or
- (8) alkynylene;

provided said compound is other than a compound of formula XIV



where

Z_e is ~~-S-~~, ~~S(O)_q-~~ or ~~CH₂-S(O)_q-~~;

Q_{2e} is phenyl optionally substituted with one group selected from halo, hydroxy, alkoxy nitro, -NH₂,
-alkyl(NH₂), -C(O)NH₂, -alkylC(O)NH₂ or -arylC(O)NH₂;

R_{e1} is H, alkyl, hydroxyalkyl, halogen or carboxy; and

R_{e2} is H, -C(O)alkyl, -SO₂alkyl or -C(O)phenyl optionally substituted with halogen.

9. A compound of claim 8 where

Z is ~~S-~~, ~~CR₄R₅-~~ or ~~S-CR₄R₅-~~;

R_2 is hydrogen or alkyl; and

R_3 is -Z₄R_{6a}, where:

- (c) Z_4 is a single bond and R_{6a} is heteroaryl optionally substituted with one or more Z_1 , Z_2 or Z_3 ;
- (d) Z_4 is -C(O)- and R_{6a} is
 - (5) aryl optionally substituted with one or more Z_1 , Z_2 or Z_3 ;
 - (6) alkyl optionally substituted with one or more Z_1 , Z_2 or Z_3 ;
 - (7) cycloalkyl optionally substituted with one or more Z_1 , Z_2 or Z_3 ; or
 - (8) heterocyclo optionally substituted with one or more Z_1 , Z_2 or Z_3 ; or
- (e) Z_4 is -C(O)-O- and R_{6a} is alkyl, cycloalkyl, aryl or aralkyl, any of which may be optionally substituted with one or more Z_1 , Z_2 or Z_3 .

17. A pharmaceutical composition comprising at least one compound of claim ~~4~~ 7 and a pharmaceutically acceptable vehicle or carrier therefor.